COVID-19 Therapeutics Information Brief

January 25, 2022

Changes to the document from the previous version are highlighted in yellow.
Next Therapeutic Information Brief will be February 2, 2022

IMPORTANT/NEW COVID-19 Therapeutics Information

Bamlanvimab/Etesevimab and REGEN-COV No Longer Authorized for Use by FDA

CDC data confirms Omicron is the overwhelmingly dominant variant of concern (VOC) in the United States at a prevalence of greater than 97.8% in all regions and nationally greater than 99%. The FDA updated the Emergency Use Authorization (EUA) fact sheets for two COVID-19 monoclonal antibody treatments: Lilly's bamlanivimab plus etesevimab and Regeneron's casirivimab plus imdevimab (REGEN-COV). **FDA now says these two treatments are not currently authorized for use anywhere in the U.S., due to the prevalence of Omicron.** FDA is encouraging healthcare providers to choose authorized treatment options with activity against circulating variants in their state, territory, or U.S. jurisdiction. This follows action last week by the National Institutes of Health (NIH) to update its clinical guidelines to recommend against the use of bamlanivimab plus etesevimab and casirivimab plus imdevimab (REGEN-COV) at this time. **Allocations will not include bamlanivimab plus etesevimab and casirivimab plus imdevimab (REGEN-COV) in this week's allocations for COVID-19 therapeutics.** Current supplies of bamlanivimab plus etesevimab and Regeneron's casirivimab plus imdevimab (REGEN-COV) should be retained by healthcare providers for potential use for other COVID variants.

Allocations for Monoclonal Antibodies, Pre-Exposure Prophylaxis Treatment and Antivirals

Iowa Statewide Allocations for the week Monday, January 24, 2022 - Sunday, January 30, 2022			
mAbs	Oral AVs		PrEP
Sotrovimab	Mulnupiravir	Paxlovid	EVUSHELD
384 doses	3,080 courses	780 courses	696 doses

Therapeutic product requests from Iowa healthcare providers continue to greatly exceed the number of therapeutic courses allocated to Iowa by the federal government. HHS has clearly stated the intent to decrease the allocation of therapeutics, specifically monoclonals, as Omicron becomes dominant across states. Iowa continues to see a decrease in allocation numbers from the federal government for BAM/ETE and REGEN-COV therapeutics. Please refer to the below talking points to ensure healthcare providers are up-to-date with the current therapeutics allocation process.

- The Iowa Department of Public Health (IDPH) is working to prioritize allocations of therapeutic products based on the regional trends of the variants.
- County by county variant rates *are not* being considered in therapeutic requests due to available data.
- **Allocations will not include bamlanivimab plus etesevimab and casirivimab plus imdevimab (REGEN-COV) in this week's allocations for COVID-19 therapeutics.**
- **Healthcare providers should NOT expect to receive regular (or any) allocations of therapeutic products.**
- **IDPH encourages entities who do receive allocations of therapeutic products to notify and work with prescribers and LPHAs on the availability of therapeutic products in the community.**
- The Therapeutic Information Brief will continue to provide the most up-to-date information regarding the availability of therapeutic products and ordering cadence.
- The Department of Health and Human Services has released a COVID-19 Therapeutics locator. Monoclonals are not well populated yet largely because of availability across the state/nation.
    - The locations displayed in the locator are based on stock on hand as reported by the location and are not a guarantee of availability.
    - Locations that report fewer than 5 courses of the selected therapeutic are not displayed. All therapeutics identified in the locator must be used in alignment with the terms of the respective product's EUA.
    - **This therapeutics locator is intended for provider use, as the included therapies require a prescription by a licensed and authorized provider. Patients should not contact locations directly.**

Disposal of Extra Doses of Nirmatrelvir from Blister Packs for Patients with low eGFR

Per Dear HCP Letter endorsed by the FDA, in reference to moderate renal impairment dosing adjusted to 150 mg nirmatrelvir with 100 mg ritonavir taken twice daily for 5 days: "Pharmacists should discard the removed tablets per state requirements or local guidelines." It is recommended providers dispose of the medication via the workflows used to dispose of expired or other waste purposes. The HCP letter and Pharmacist Instructions are available at: https://www.covid19oralrx-hcp.com/resources.

COVID-19 Treatment Guidelines When There Are Logistical or Supply Constraints

The purpose of this interim statement is to provide guidance on which individuals might receive the greatest benefit from anti-SARS-CoV-2 therapeutics for treatment or prevention.

Prioritization:

- Treatment of COVID-19 over post-exposure prophylaxis (PEP) of SARS-CoV-2 infection
- Treatment of COVID-19 in unvaccinated or incompletely vaccinated individuals with clinical risk factors for severe illness and vaccinated individuals who are not expected to mount an adequate immune response
- Use of tixagevimab plus cilgavimab (Evusheld) as pre-exposure prophylaxis (PrEP) for severely immunocompromised individuals over moderately immunocompromised individuals

Tier	Risk Group
1	Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status (see Immunocompromising Conditions below); *or* Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors).
2	Unvaccinated individuals at risk of severe disease not included in Tier 1 (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors)
3	Vaccinated individuals at high risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with clinical risk factors) **Note:** Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.
4	Vaccinated individuals at risk of severe disease (anyone aged ≥65 years or anyone aged <65 with clinical risk factors) **Note:** Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.

https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-patient-prioritization-for-outpatient-therapies/

Patient Prioritization for Outpatient Anti-SARS-CoV-2 Therapies With Supply Constraints

The COVID-19 Treatment Guidelines Panel (the Panel) has recommended several therapeutic agents for the treatment and prevention of SARS-CoV-2 infection in individuals who are at high risk for progression to severe COVID-19. With the increase in cases of COVID-19 and the emergence of the Omicron (B.1.1.529) variant of concern, there are supply constraints that make it impossible to offer the available therapy to all eligible patients, making patient triage necessary. When supply constraints limit the availability of anti-SARS-CoV-2 mAbs or small molecule antivirals, the Panel recommends clinicians prioritize the use of therapeutics for patients at highest risk of clinical progression.

Purpose of This Statement

The purpose of this statement is to provide clinicians with guidance on the use of ritonavir-boosted nirmatrelvir (Paxlovid), sotrovimab, remdesivir, and molnupiravir for the treatment of nonhospitalized patients with COVID-19 who are at high risk of progressing to severe disease. These recommendations are based on the results of clinical trials for ritonavir-boosted nirmatrelvir (Paxlovid), remdesivir, and molnupiravir, and on the results of clinical trials and laboratory assessments of the activity of the anti-SARS-CoV-2 mAb products that are currently available through EUAs for COVID-19 treatment.

It should be noted a number of factors affect the selection of the best treatment option for a specific patient. These factors include, but are not limited to, the clinical efficacy of the treatment option, the availability of the treatment option, the feasibility of administering parenteral medications (i.e., sotrovimab, remdesivir), the potential for significant drug-drug interactions (i.e., the interactions associated with using ritonavir-boosted nirmatrelvir [Paxlovid]), and the regional prevalence of the Omicron VOC.

Recommendations (Listed in order of preference)

For nonhospitalized patients with mild to moderate COVID-19 who are at high risk of disease progression, the Panel recommends using 1 of the following therapeutics:

Nirmatrelvir 300 mg with ritonavir 100 mg (Paxlovid) orally twice daily for 5 days, initiated as soon as possible and within 5 days of symptom onset in those aged ≥12 years and weighing ≥40 kg (AIIa).

- Ritonavir-boosted nirmatrelvir (Paxlovid) has significant and complex drug-drug interactions, primarily due to the ritonavir component of the combination.
- Before prescribing ritonavir-boosted nirmatrelvir (Paxlovid), clinicians should carefully review the patient's concomitant medications, including over-the-counter medications and herbal supplements, to evaluate potential drug-drug interactions. See the Panel's statement on the drug-drug interactions for ritonavir-boosted nirmatrelvir (Paxlovid) for details.

Sotrovimab 500 mg as a single IV infusion, administered as soon as possible and within 10 days of symptom onset in those aged ≥12 years and weighing ≥40 kg who live in areas with a high prevalence of the Omicron VOC (AIIa).

- If the Delta VOC still represents a significant proportion of infections in the region and other options are not available or are contraindicated, patients can be offered bamlanivimab plus etesevimab or casirivimab plus imdevimab, with the understanding that this treatment would be ineffective if they are infected with the Omicron VOC.
- Sotrovimab should be administered in a setting where severe hypersensitivity reactions, such as anaphylaxis, can be managed. Patients should be monitored during the infusion and observed for at least 1 hour after infusion.

Remdesivir 200 mg: The FDA has expanded the approved indication for Veklury to include its use in adults and pediatric patients (12 years of age and older who weigh at least 40 kilograms, which is about 88 pounds) with positive results of direct SARS-CoV-2 viral testing, and who are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

- The agency also revised the Emergency Use Authorization (EUA) for Veklury to additionally authorize the drug for treatment of pediatric patients weighing 3.5 kilograms to less than 40 kilograms or pediatric patients less than 12 years of age weighing at least 3.5 kilograms, with positive results of direct SARS-CoV-2 viral testing, and who are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization of death. These high-risk non-hospitalized patients may receive Veklury via intravenous infusion for a total of three days for the treatment of mild-to-moderate COVID-19 disease.
- Remdesivir EAU Letter of Authorization
- Healthcare Provider Fact Sheet
- Parents/Caregiver Fact Sheet

Molnupiravir 800 mg orally twice daily for 5 days, initiated as soon as possible and within 5 days of symptom onset in those aged ≥18 years **ONLY** when none of the above options can be used (CIIa).

- The FDA EUA states that molnupiravir is not recommended for use in pregnant patients due to concerns about the instances of fetal toxicity observed during animal studies. However, when other therapies are not available, pregnant people with COVID-19 who are at high risk of progressing to severe disease may reasonably choose molnupiravir therapy after being fully informed of the risks, particularly those who are beyond the time of embryogenesis (i.e., >10 weeks' gestation). The prescribing clinician should document that a discussion of the risks and benefits occurred and that the patient chose this therapy.
- There are no data on the use of molnupiravir in patients who have received COVID-19 vaccines, and the risk-to-benefit ratio is likely to be less favorable because of the lower efficacy of this drug.

FDA Expands Use of VEKLURY™ (remdesivir)

Gilead's product - VEKLURY™ (remdesivir), is not allocated by the federal government but is available commercially. The U.S. Food and Drug Administration took two actions to expand the use of the antiviral

remdesivir to certain non-hospitalized adults and pediatric patients for the treatment of mild-to-moderate COVID-19 disease. This provides another treatment option to reduce the risk of hospitalization in high-risk patients. Previously, the use of Veklury was limited to patients requiring hospitalization.

The FDA has expanded the approved indication for remdesivir to include its use in adults and pediatric patients (12 years of age and older who weigh at least 40 kilograms, which is about 88 pounds) with positive results of direct SARS-CoV-2 viral testing, and who are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

The agency also revised the Emergency Use Authorization (EUA) for Veklury to additionally authorize the drug for treatment of pediatric patients weighing 3.5 kilograms to less than 40 kilograms or pediatric patients less than 12 years of age weighing at least 3.5 kilograms, with positive results of direct SARS-CoV-2 viral testing, and who are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization of death.

Pediatric patients for whom remdesivir is authorized will receive doses adjusted for their body weight in order to achieve comparable exposures to adults and pediatric patients receiving the approved dose. Given the similar course of COVID-19 disease, the authorization of remdesivir in certain pediatric patients is based on extrapolation of efficacy from adequate and well-controlled studies in adults.

- Remdesivir EAU Letter of Authorization
- Healthcare Provider Fact Sheet
- Parents/Caregiver Fact Sheet

COVID-19 Treatment Guidelines - Evusheld

COVID-19 Treatment Guidelines Panel recommends using **tixagevimab plus cilgavimab** as SARSCoV-2 PrEP for adults and adolescents (aged ≥12 years and weighing ≥40 kg) who do not have SARS-CoV-2 infection, who have not been recently exposed to an individual with SARS-CoV-2 infection, **AND** who:

- are moderately to severely immunocompromised and may have an inadequate immune response to COVID-19 vaccination; or
- are not able to be fully vaccinated with any available COVID-19 vaccines due to a documented history of severe adverse reactions to a COVID-19 vaccine or any of its component.

- If supplies of tixagevimab plus cilgavimab are limited, priority should be given to those who are at the highest risk for severe COVID-19 (see the Panel's statement on prioritizing patients for outpatient therapies when there are logistical or supply constraints).

- **Using tixagevimab plus cilgavimab as SARS-CoV-2 PrEP is NOT AUTHORIZED by the FDA in unvaccinated individuals for whom COVID-19 vaccination is recommended.**

Therapeutic Reporting Reminder

The Iowa Department of Public Health (IDPH) will be closely monitoring and tracking inventory and administration of COVID-19 therapeutics distributed to Iowa healthcare provider organizations. The need for accurate reporting of therapeutics will be greater than ever to ensure timely utilization of therapeutic products. The redistribution of COVID-19 therapeutics beyond the primary distribution locations is acceptable and necessary to ensure availability.

Sites receiving monoclonal antibodies, pre-exposure prophylaxis treatment, or oral antivirals **MUST** comply with federal reporting requirements.
Failure to comply with reporting requirements may result in the loss of COVID-19 therapeutic providers status and removal of COVID-19 therapeutic products. Reporting requirements are as follows:

- Monoclonal antibodies (REGEN-COV, bamlanivimab/etesevimab, sotrovimab): Report on-hand and usage data **every Wednesday** in EMResource (for hospitals), NHSN (for long-term care facilities), or Teletracking (for all other sites).
- Pre-exposure prophylaxis treatment or oral antivirals (Evusheld, Paxlovid, Molnupiravir): Report on-hand and usage data **daily** in HPoP. If you need assistance with HPoP, please contact c19therapeutics@idph.iowa.gov.

Redistribution Requests for Therapeutics

Requests have been received regarding redistribution of monoclonal antibodies, evusheld and antivirals. Healthcare providers wanting to redistribute antivirals (Paxlovid, Molunpiravir) and pre-exposure prophylaxis (Evusheld) must email the IDPH Therapeutics Call Center at C19Therapeutics@idph.iowa.gov to initiate the redistribution process. **Do not redistribute any doses or courses of antivirals (Paxlovid, Molunpiravir) and pre-exposure prophylaxis (Evusheld) without contacting the Therapeutics Call Center prior to physically transferring.**

At this time, monoclonal antibodies do not require IDPH approval for redistribution. Healthcare providers may continue the current practice of monoclonal antibodies redistribution. In the future, monoclonal antibodies may be incorporated into this redistribution policy.

Weekly Allocations Cadence for Monoclonal Antibodies, Pre-Exposure Prophylaxis Treatment and Antivirals

IDPH *anticipates* a weekly allocation cycle through January for the allocation cadence of monoclonal antibodies (REGEN-COV, bamlanivimab/etesevimab, sotrovimab) and the pre-exposure prophylaxis treatment (Evusheld). The ordering cadence will be as follows:

- Allocation Survey Sent - Monday
- Allocation Survey Due Back to IDPH - Tuesday at 4:00pm
- Allocation Ordered in Federal System - Thursday

- Allocation Amount Notification from IDPH to healthcare providers - Thursday

IDPH *anticipates* an every other week allocation cycle through January for the allocation cadence of antivirals. The next allocation for antivirals products will be the week of January 10, 2022. The ordering cadence will be as follows:

- Allocation Survey Sent - Monday
- Allocation Survey Due Back to IDPH - Tuesday at 4:00pm
- Allocation Ordered in Federal System - Thursday
- Allocation Amount Notification from IDPH to healthcare providers - Thursday

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Oral COVID-19 Therapeutics Pharmacy Coverage Informational Letter from Iowa Department of Human Services (DHS), Iowa Medicaid Enterprise (IME)

The link below is to an informational letter updating providers regarding the appropriate billing and coding fees for the use of two oral antivirals for treatment of COVID-19 under an emergency use authorization (EUA).

- Oral COVID-19 Therapeutics Pharmacy Coverage Informational Letter, January 2022

The link below references coverage of over the counter anti-viral information on the HRSA website and correlating FAQs.

- https://www.hrsa.gov/CovidUninsuredClaim
- https://www.hrsa.gov/coviduninsuredclaim/frequently-asked-questions

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Allocations for Monoclonal Antibodies, Pre-Exposure Prophylaxis Treatment and Oral Antivirals

Local Public Health Agencies and Hospital Partners should refer to the Iowa Health Alert Network (HAN) Therapeutics folder-partner list for the spreadsheet listing the facilities that have been allocated therapeutics for each type of product.

COVID-19 Therapeutics Information Resources

- **COVID-19 Therapeutics Call Center -** IDPH has established a COVID-19 Therapeutics Call Center. To reach the COVID-19 Therapeutics Call Center, call **515-281-7317**.
- **COVID-19 Therapeutics Email -** IDPH has set up a COVID-19 Therapeutics Email to respond specifically to questions from healthcare providers regarding COVID-19 therapeutics. Therapeutic questions can be emailed to: C19Therapeutics@idph.iowa.gov
- NOTE: **The COVID-19 Therapeutics Call Center and Email are intended for healthcare providers only.**
- **COVID-19 Therapeutics Website -** IDPH is in the process of updating the COVID-19 Therapeutics website with additional resources. Information will be shared as soon as it is available.

COVID-19 Therapeutics Table

	mAbs	Oral Antivirals		PrEP
Products	**Sotrovimab (GSK)**	**Molnupiravir (Merck)**	**Paxlovid (Pfizer)**	**Tixagevimab/Cilgavimab (EVUSHELD)**
Authorized Use(s)	Treatment of mild to moderate symptoms	Treatment of mild to moderate symptoms	Treatment of mild to moderate symptoms	Pre-exposure prevention for immunocompromised individuals
Age Eligibility	Ages 12 years and older	Ages 18 and older	Ages 12 years and older	Ages 12 years and older
Weight Eligibility	88 pounds or more	No weight requirement	88 pounds or more	88 pounds or more
Other Criteria for Treatment	Test Positive for SARS-CoV-2 Be within **10** days of the start of symptoms Not be hospitalized	Test Positive for SARS-CoV-2 Be within **5** days of the start of symptoms Not be hospitalized	Test Positive for SARS-CoV-2 Be within **5** days of the start of symptoms Not be hospitalized	**Not currently infected with SARS-CoV-2** Have not had a known recent exposure to an infected individual with SARS-CoV-2
Other Criteria for Prevention				Must have moderate to severe immune compromise due to a medical condition diagnosed by a health care provider
Letter of Authorization	Sotrovimab Letter of Authorization (EUA)	Molnupiravir EUA Letter of Authorization	Paxlovid EUA Letter of Authorization	Evusheld EUA Letter of Authorization (EUA)
EUA Fact Sheet	Sotrovimab Provider Fact Sheet	Molnupiravir Provider Fact Sheet	Paxlovid Provider Fact Sheet	Evusheld Provider Fact Sheet